Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Prior to the present amendment, claims 39-51 were pending in this application and were rejected on various grounds. Claim 48 has been canceled without prejudice and claims 39-44 has been amended. The rejection to the presently pending claims are respectfully traversed.

Sequence Compliance

2. Applicants have deleted the sequences on page 2, line 37 and page 14, line 17 to overcome this objection.

Oath/Declaration

Applicants have enclosed a new combined declaration executed by Wei-Qiang Gao to overcome this objection.

Specification

5. The specification has been objected to for containing an embedded hyperlink. The foregoing amendment, which deleted all embedded hyperlinks or other forms of browser executable code, is believed to overcome this objection.

6. Applicants submit that Table 1 is a computer program while Tables 2-6 comply with 37 C.F.R. 1.55(c) format.

Claim Rejections – 35 USC § 101

7. Claims 39-51 were rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility." The Examiner specifically noted that "the instant specification does not disclose a credible "real world" use for the encoded protein encoded then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful."

The rejection is respectfully traversed.

Utility – Legal Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is

probative of the applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

Applicants rely on the proinflammatory cell infiltration assay (Example 77) to establish patentable utility for the polypeptide PRO331. These results were first disclosed in international application PCT/US98/19437, filed 17 September, 1998 to which priority is claimed in this application. Support is present in the present application in Example 77, page 210, lines 22 onwards. Accordingly, the present application is entitled to the effective filing date of 17 September, 1998.

Present claim amendments recite polypeptides "capable of inducing an immune or inflammatory response." Support for this recitation is found in Example 77 (page 210, lines 22) which describes a dye-based proinflammatory cell infiltration assay in which PRO331 induces mononuclear cell, eosinophil and PMN infiltration into the site of injection of this peptide/protein into an animal.

In the proinflammatory cell infiltration assay, purified or conditioned media containing PRO331 was injected intradermally onto the backs of hairless guinea pigs whereas the Evans blue dye was injected intracardially. Blemishes at the injection sites were measured 1 h and 6 h post injection. Animals were sacrificed at 6 h after injection, the skin at each injection site was biopsied, fixed in formalin and evaluated histopathologically for inflammatory cell infiltration into the skin. Such inflammatory cell infiltration assays are routinely used in the art to evaluate proinflammatory properties of novel compounds (see Rampart et al; enclosed in IDS). For example, in Rampart et al., IL-8 (Interleukin 8) was identified using a neutrophil accumulation assay in rabbit skin (see Methods, page 22) and the findings were correlated with albumin flux and neutrophil dependent edema in skin.

During proinflammatory conditions, several mechanisms act synergistically to mediate an increase in neutrophil accumulation, plasma extravasation, etc. Such events occur for example, during the acute phase of an inflammatory response to a microbial stimulus or during pathologic conditions like graft rejection, edema, psoriasis, arthritis, tissue injury etc. For example, the enclosed reference, Rampart et al. indicates that endogenous IL-8 could be involved in the acute phase of an inflammatory response to a microbial stimulus and further disclosed suggestive data to support its involvement in psoriatic patients (see page 24, column 1, last paragraph). Subsequent knowledge in the art has shown many important biological roles for IL-8; for example: IL-8 has been shown to be part of the cytokine cascade in the synovium of patients suffering from rheumatoid arthritis; further, IL-8 is associated with other inflammatory diseases like asthma, leprosy, psoriasis, inflammatory bowel disease, atherosclerosis, cystic fibrosis, and in various respiratory syndromes. IL-8 has been shown to induce tumor growth, an effect attributed to its angiogenic activity while administration of anti–IL-8 to SCID mice bearing xenografts of IL-8–expressing human lung cancer has been shown to have beneficial effects. Similarly, a variety of real-life utilities are envisioned for PRO331 based on the proinflammatory cell infiltration assay results.

Accordingly, agents capable of inducing inflammatory cell infiltration like PRO331, can be used, for example, to therapeutically boost an immune response in a given target tissue and are therefore, promising drug candidates for the same. Alternatively, antibodies raised against PRO331 can be exploited for anti-inflammatory therapy and could also be useful as diagnostic agents in identifying pathologic conditions associated with inflammation like psoriasis, graft rejection, arthritis, etc.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. Indeed, the logic underlying Applicants' assertion that PRO266 may be useful in boosting an immune response is not inconsistent with the general knowledge in the art, and would be considered credible by a person skilled in the art. It is always possible that an

invention might fail on its way of development to a commercial product. For example, despite recent advances in rational drug design, a large percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections – 35 USC § 112/Enablement and Written Description

8. Claims 39-51 were rejected under 35 U.S.C. §112, first paragraph, since allegedly, the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, thus one skilled in the art would not know how to use the claimed invention. Applicants respectfully traverse.

9. Claims 39-43 were rejected under 35 U.S.C. §112, first paragraph, as allegedly, containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

A specific and substantial asserted utility is now recited in the rejected claims wherein the PRO266 polypeptides are "capable of inducing an immune or inflammatory response." Based on the information disclosed in the specification and that available in the art, one skilled in the art knew how to practice the claimed invention, at the effective priority date of this application, without undue experimentation. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174* (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01. Further, since the claims are now drawn to a genus of polypeptides defined by sequence and functional identity as well, one skilled

in the art knew, at the effective priority date of this application, that the Applicants possessed the claimed sequences.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of all pending claims under this section.

10. Claims 39-44 and 49 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner says that the deposit requirements for plasmid and/or microorganism is not fulfilled in accordance with 37 C.F.R. 1.801-1.809.

Present amendments to the specification at page 251, line 10 have incorporated assurances that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent."

Accordingly, a person in the art would have access to the deposit made and hence, the present rejection should be withdrawn.

35 USC § 112, Second Paragraph

Claims 39-51 were rejected under 35 U.S.C. §112, second paragraph, allegedly, as being indefinite for reciting "the polypeptide...lacking its associated signal peptide" and "the extracellular domain...lacking its associated signal sequence, parts (b) and (d)." Claims 45 and 49-52 were indefinite for being dependent from indefinite claims.

The foregoing amendments wherein such references have been deleted in the above claims are believed to overcome this rejection. Further, Claims 45 and 49-52 now depend from definite claims. Hence, these rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C29). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: May 27, 2003

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